DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

# Memorandum

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Date: JAN 22 2008

From: Consumer Safety Officer, Division of Dietary Supplement Programs , Office of Nutritional Products, Labeling and Dietary Supplements, HFS-810

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

Subject of the Notification: Hyaluronic acid or Sodium Hyaloronate

Firm: Aquaflex, Inc.

Date Received by FDA: September 7, 2007

90-Day Date: December 6, 2007

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification and related correspondence for the aforementioned substance should be placed on public display in docket number 95S-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

*Theresa Prigmore*

(95S-0316)

(Rpt 426)

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
5100 Paint Branch Parkway
College Park, Maryland 20740

SEP 14 2007

Elizabeth Sherman
Director of Quality Control/Regulatory
Bell Pharmaceuticals, Inc.
4525 Hiawatha Avenue
Minneapolis, Minnesota 55406

Dear Ms. Sherman:

This is to inform you that the notification which you submitted pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on August 21, 2007. Additional information was received on September 7, 2007. Your notification concerned "Hyaluronic Acid, otherwise known as Sodium Hyaluronate" which you identify as a new dietary ingredient that is biosynthesized by fermentation of microorganisms.

According to your notification, "Hyaluronic Acid [will be used in]... an artificially flavored drink called Aquaflex that will be sold in 4 different flavors." In addition, "(a)ll four flavors contain 48 mg of Hyaluronic Acid per 8 oz serving. The daily recommended dose of Hyaluronic Acid is one 20 oz bottle per day with a total of 120 mg of Hyaluronic Acid."

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under 21 U.S.C. 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

Under 21 CFR 190.6(5)(d) if the manufacturer or distributor of a dietary supplement that contains a new dietary ingredient, or of the new dietary ingredient, provides additional information in support of the new dietary ingredient notification, the agency will review all

submissions pertaining to that notification, including responses made to inquiries from the agency, to determine whether they are substantive and whether they require that the 75-day period be reset. If the agency determines that the new submission is a substantive amendment, FDA will assign a new filing date. FDA will acknowledge receipt of the additional information and, when applicable, notify the manufacturer of the new filing date, which is the date of receipt by FDA of the information that constitutes the substantive amendment.

This letter is to inform you that the agency has determined that the material received on September 7, 2007 is a substantive amendment to the previously received notification and has accordingly reset the 75-day period based on the new filing date of September 7, 2007.

Your notification will be kept confidential for 90 days after the filing date of September 7, 2007. After the 90-day date, the notification will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. Prior to that date, you may wish to identify in writing specifically what information you believe is proprietary, trade secret or otherwise confidential for FDA's consideration.

If you have any questions concerning this matter please contact me at (301) 436-1448.

Sincerely yours,

Linda S. Pellicore

Linda S. Pellicore, Ph.D.
Manager/Supervisor, Senior Toxicologist
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety and Applied Nutrition

DEPARTMENT OF HEALTH AND HUMAN SERVICES

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5100 Paint Branch Parkway
College Park, Maryland 20740

DEC 14 2007

Elizabeth Sherman
Director of Quality Control/Regulatory
Microbiologist
Bell Pharmaceuticals, Inc.
4525 Hiawatha Ave.
Minneapolis, Minnesota 55406

Dear Ms. Sherman:

This is to inform you that the notification dated August 14, 2007 which you submitted on behalf of Aquaflex, Inc. pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on August 21, 2007. Additional material was received on September 7, 2007. On September 14, 2007, FDA informed you that the material received on September 7 was a substantive amendment to your notification and reset the 75-day period based on the new filing date of September 7, 2007. Your notification concerned "Hyaluronic Acid, otherwise known as Sodium Hyaluronate" which you identify as a new dietary ingredient.

According to your notification, "Aquaflex, Inc is putting Hyaluronic Acid into an artificially flavored drink called Aquaflex that will be sold in 4 different flavors. It also states that the drink "contain 48 mg of Hyaluronic Acid per 8 oz serving. The daily recommended dose of Hyaluronic Acid is one 20 oz bottle per day with a total of 120 mg of Hyaluronic Acid."

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under 21U.S.C.350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21U.S.C.342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

Your product is excluded from the definition of "dietary supplement" under 21 U.S.C. 321(ii)(3)(B). Hyaluronic Acid is an article authorized for investigations as a drug for which substantial clinical investigations have been instituted in the United States and the investigations have been made public. In addition, your notification provides no evidence that

"Hyaluronic Acid, otherwise known as Sodium Hyaluronate" was marketed as a dietary supplement or as a food prior to the authorization to investigate "Hyaluronic Acid" as a new drug. Moreover, your notification states that the injectable form of "Hyaluronic Acid" is registered to the FDA as a medical device.

In summary, "Hyaluronic Acid" is not a dietary supplement under the Federal Food, Drug and Cosmetic Act. Moreover, the product appears to be a drug under the Act and thus subject to the regulatory requirements of drugs.

Your notification will be kept confidential for 90 days after the filing date September 7, 2007. After the 90-day date, the notification will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. Prior to that date, you may wish to identify in writing specifically what information you believe is proprietary, trade secret or otherwise confidential for FDA's consideration.

If you have any questions concerning this matter please contact me at (301) 436-1448.

Sincerely yours,

Linda S. Pellicore

Linda S. Pellicore, Ph.D.
Supervisory Team Leader, Senior Toxicologist
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety and Applied Nutrition

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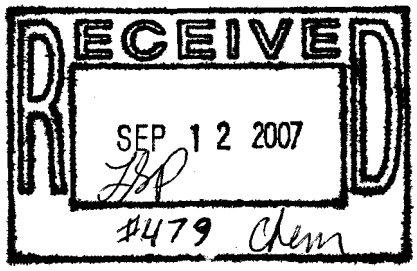
Aquaflex, Inc.
7 west 36th Street, 15th Floor
New York, New York 10018




August 14, 2007

Food and Drug Administration
Office of Nutritional Products,
Labeling and Dietary Supplements (HFS-820)
Center for Food Safety and Applied Nutrition
5100 Paint Branch Parkway
College Park, MD 20740

Dear Sirs:

In accordance with Section 8 of the Dietary Supplement Health and Education Act of 1994 and Federal code of regulation 21 cfr 190.6, Aquaflex, Inc. submits this notification and information concerning a dietary ingredient that Aquaflex intends to market for use in a new dietary supplement. Pursuant to the provisions of the regulations Aquaflex will not introduce or deliver the supplement into interstate commerce until at least 75 days after the date the FDA receives this notification.

1. Name and Address of Manufacture and Distributor of the Dietary Supplement

   The name and address of the manufacturer of the new dietary supplement is as follows:

   Bell Pharmaceuticals, Inc
   200 W. Beaver Street
   Belle Plaine, MN 56011
   Phone: (952) 873-2288

   Mailing address:
   Bell Pharmaceuticals, Inc.
   PO Box 128
   Belle Plaine, MN 56011

   The name and address of the distributor of the new dietary supplement is as follows:

   Aquaflex, Inc.
   7 West 36th Street, 15th Floor
   New York, New York 10018
   Phone: (212) 736-2310

2. Name of the New Dietary Ingredient

   The name of the new dietary ingredient is Hyaluronic Acid, otherwise known as Sodium Hyaluronate.

Aquaflex, Inc.
7 west 36th Street, 15th Floor
New York, New York 10018

3. Description of the Dietary Supplement

Aquaflex, Inc is putting Hyaluronic Acid into an artificially flavored drink called Aquaflex that will be sold in 4 different flavors. Maintain will be an orange tangerine flavor. Recover will be a raspberry flavor. Perform will be a lemonade flavor. Defend will be a grape flavor with added vitamin A, vitamin B12, niacin and vitamin E. All four flavors contain 48 mg of Hyaluronic Acid per 8 oz serving. The daily recommended dose of Hyaluronic Acid is one 20 oz bottle per day with a total of 120 mg of Hyaluronic Acid.

The Hyaluronic acid being used in this dietary supplement is biosynthesized by fermentation of microorganisms. The molecular formula is (C14H20NnaO11)n where n represents the number of chains in the Hyaluronic acid molecule. The CAS number is 9067-32-7.

4. The History of Use or Other Evidence of Safety for the Dietary Ingredient

Hyaluronic acid has a history of use in the United States. One form is an injectable form of Hyaluronic acid registered to the FDA as a medical device under the names Hyalgan, Supartz and Synvisc. This form was first registered with the FDA in 1997 and is approved for the treatment of osteoarthritis. Hyaluronic acid is also sold as a dietary supplement in capsule, tablet and serum form.

Hyaluronic acid is naturally occurring substance found in synovial fluid. Synovial fluid depends upon Hyaluronic acid for its viscoelacticity and therefore its lubricating properties. Hyaluronic acid has a low incidence of side-effects (Huskisson et. Al, 1999).

We trust that this dietary ingredient submission provides all the information the FDA requires. If there are any questions concerning this submission, please call me at (612) 721-3976 x 112 or contact me at the address below.

Sincerely,

Elizabeth Sherman
Bell Pharmaceuticals, Inc
Director of Quality Control/Regulatory
Microbiologist
4525 Hiawatha Ave
Minneapolis, MN 55406
esherman@bellpharm.com

cc: M.E. Saremi CEO/Chemist
Harley Blattner
William Christopfel
Dr. Steve Allday
Marc Wexler

enclosure